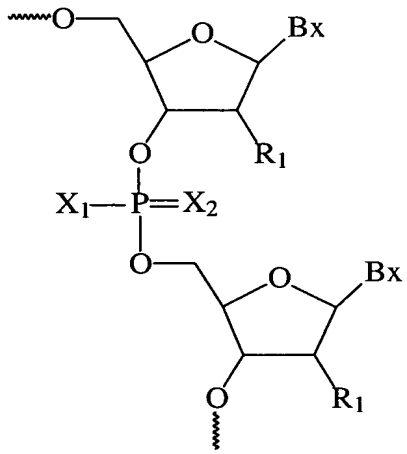
WHAT IS CLAIMED IS:

1. A method of preparing an oligomeric compound having at least one moiety of formula:



wherein:

X_2 is O or S;

X_1 is Pg-O-, Pg-S-, C_1-C_{10} straight or branched chain alkyl, $CH_3(CH_2)_{nn}$-O-, R_2R_3N- or a group remaining from coupling a chiral auxiliary;

nn is from 0 to 10;

Pg is CH_3, $-CH_2CH_2CN$, $-C(CH_3)(CH_3)-CCl_3$, $-CH_2-CCl_3$, $-CH_2CH=CH_2$, $CH_2CH_2SiCH_3$, 2-yl-ethyl phenylsulfonate, δ-cyano-butenyl, cyano *p*-xylyl, diphenylsilylethyl, 4-nitro-2-yl-ethylbenzene, 2-yl-ethyl-methyl sulfonate, methyl-N-trifluoroacetyl ethyl, acetoxy phenoxy ethyl, or a blocking group;

each R_2 and R_3 is, independently, hydrogen, C_1-C_{10} alkyl, cycloalkyl or aryl;

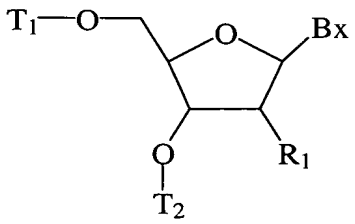
or optionally, R_2 and R_3, together with the nitrogen atom to which they are attached form a cyclic moiety;

each Bx is, independently, a heterocyclic base moiety; and

each R_1 is, independently, H, a blocked hydroxyl group, or a sugar substituent group;

comprising the steps of:

(a) providing a 5'-O-protected compound of the formula:



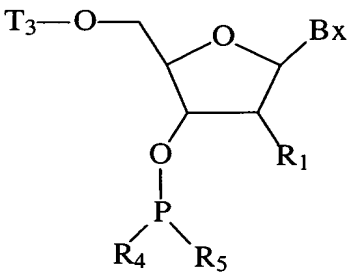
wherein:

T_1 is a hydroxyl protecting group; and

T_2 is a covalent attachment to a support media, a nucleoside bound to a support media, a nucleotide, an oligonucleoside or an oligonucleotide;

(b) treating said 5'-O-protected compound with a deprotecting reagent for a time and under conditions effective to form a 5'-O-deprotected compound;

(c) coupling said 5'-O-deprotected compound with an activated phosphorus composition of the formula:



wherein:

T_3 is a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleoside or an oligonucleotide;

R_4 is $N(L_1)L_2$;

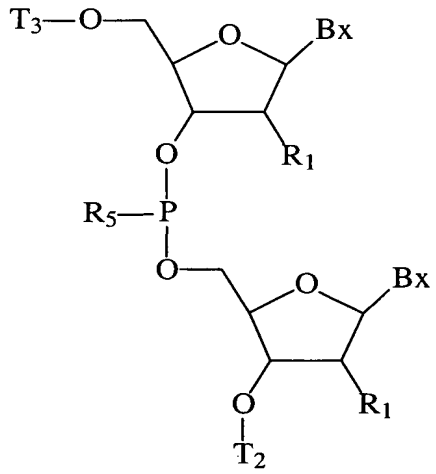
each L_1 and L_2 is, independently, C_{1-6} straight or branched alkyl, or a C_{5-7} cyclic aliphatic ring system;

or L_1 and L_2 are joined together to form a 4- to 13-membered heterocyclic ring system including the nitrogen atom to which L_1 and L_2 are attached; and

R_5 is X_1;

or R_4 and R_5 together with the phosphorus atom to which R_4 and R_5 are attached form a chiral auxiliary;

for a time and under conditions effective to form an extended compound having the formula:



(d) treating said extended compound with a mixture comprising an oxidizing reagent and a capping reagent for a time and under conditions effective to form said oligomeric compound.

2. The method of claim 1 further comprising treating said oligomeric compound with a reagent for a time and under conditions effective to remove said blocking groups thereby forming a deblocked oligomeric compound.

3. The method of claim 2 wherein said reagent is effective to cleave the oligomeric compound from the support media.

4. The method of claim 3 wherein said reagent is aqueous ammonium hydroxide.

5. The method of claim 2 further comprising treating said oligomeric compound with a further reagent for a time

and under conditions effective to cleave the oligomeric compound from the support media.

6. The method of claim 1 further comprising treating said oligomeric compound with a deprotecting reagent for a time and under conditions effective to deprotect the T_3 hydroxyl protecting group.

7. The method of claim 1 wherein said mixture comprises from 0.02M to 0.2M oxidizing reagent.

8. The method of claim 7 wherein said mixture comprises from 0.1M to 0.2M oxidizing reagent.

9. The method of claim 1 wherein said oxidizing reagent transfers an oxygen atom.

10. The method of claim 9 wherein said oxidizing reagent is iodine, *m*-chloroperbenzoic acid, iodobenzene diacetate, tetra-*n*-butylammonium periodate, *tert*-butyl hydroperoxide, di-*tert*-butyl hydroperoxide, cumene hydroperoxide, hydrogen peroxide; bis-trimethylsilyl peroxide; dinitrogen tetroxide, oxone, molecular oxygen, (1*S*)-(+)-(10-camphorsulfonyl)oxaziridine or a peracid.

11. The method of claim 10 wherein said oxidizing reagent is iodine, *m*-chloroperbenzoic acid, iodobenzene diacetate, *tert*-butyl hydroperoxide, di-*tert*-butyl hydroperoxide, hydrogen peroxide, oxone, molecular oxygen or a peracid.

12. The method of claim 1 wherein said oxidizing reagent transfers a sulfur atom.

13. The method of claim 12 wherein said oxidizing reagent is 3-amino-1,2,4-dithiazole-5-thione; 3-ethoxy-1,2,4-dithiazoline-5-one; 1,2,4-dithiazolidine-3,5-dione; 3-methyl-1,2,4-dithiazolin-5-one; or dimethylthiuram disulfide.

14. The method of claim 13 wherein said oxidizing reagent is dimethylthiuram disulfide.

15. The method of claim 1 wherein said capping reagent comprises about one part by volume of either acetic anhydride in acetonitrile or tetrahydrofuran; or chloroacetic anhydride in acetonitrile or tetrahydrofuran; added to about one part by volume of either N-methylimidazole and pyridine in acetonitrile or tetrahydrofuran; or *t*-butylphenoxyacetic anhydride in acetonitrile or tetrahydrofuran.

16. The method of claim 15 wherein said capping reagent comprises about one part by volume of 20% acetic anhydride in acetonitrile mixed with about one part by volume of a solution having 20% N-methylimidazole, 30% pyridine and 50% acetonitrile.

17. The method of claim 1 wherein said mixture comprises dimethylthiuram disulfide, acetic anhydride, acetonitrile, N-methyl imidazole and pyridine.

18. The method of claim 1 wherein said mixture comprises from about 0.05M to 0.2M dimethylthiuram disulfide, about 10% acetic anhydride, about 10% N-methyl imidazole and about 15% pyridine in a suitable solvent.

19. The method of claim 18 wherein said solvent is acetonitrile, toluene, ethyl acetate, tetrahydrofuran,

dichloromethane, dichloroethane, dioxane, dimethylacetamide and dimethylformamide.

20. The method of claim 1 wherein said coupling of the 5'-O-deprotected compound with the activated phosphorus composition is performed in the presence of an activating agent.

21. The method of claim 20 wherein said activating agent is 1-H-tetrazole or 4,5-dicyanoimidazole.

22. The method of claim 1 where said cyclic moiety is morpholino or phthalimido.

23. The method of claim 1 wherein each L_1 and L_2 is C_{1-6} alkyl.

24. The method of claim 23 wherein each L_1 and L_2 is isopropyl.

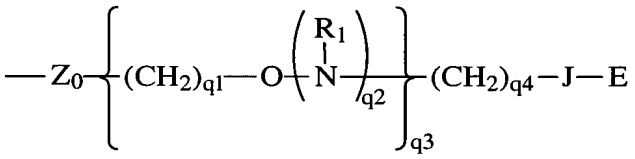
25. The method of claim 1 wherein L_1 and L_2 are joined together to form a heterocyclic ring system including the nitrogen atom to which said L_1 and L_2 are attached, wherein said ring system optionally includes at least one additional heteroatom selected from O, N and S.

26. The method of claim 25 wherein said heterocyclic ring system is morpholino.

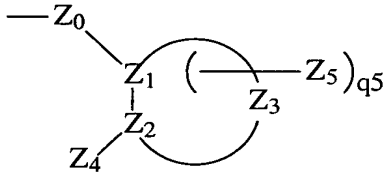
27. The method of claim 1 wherein each of said substituent groups is, independently, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_2-C_{20} alkynyl, C_5-C_{20} aryl, O-alkyl, O-alkenyl, O-alkynyl, O-aryl, O-aralkyl, O-alkylamino, O-alkylaminoalkyl (O-alkyl-N(H)alkyl), O-alkylaminodialkyl (O-alkyl-N-

$(alkyl)_2$), O-alkylalkoxy (O-alkyl-O-alkyl), O-alkyl-(N-imidazole), thiol, S-alkyl, S-alkenyl, S-alkynyl, NH-alkyl, NH-alkenyl, NH-alkynyl, N-dialkyl, S-aryl, NH-aryl, S-aralkyl, NH-aralkyl, N-phthalimido, halogen keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, N-imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, heterocycle, carbocycle, polyamine, polyamide, polyalkylene glycol, or polyether;

or, alternatively, one or more substituent groups has one of formula I or II:



I



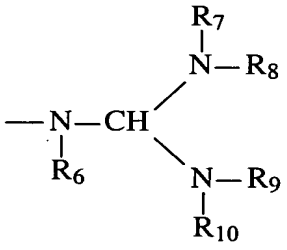
II

wherein:

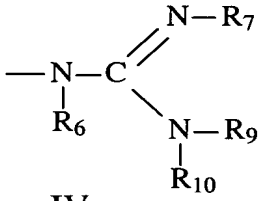
Z_0 is O, S or NH;

J is a single bond, O or C(=O);

E is C_1-C_{10} alkyl, $N(R_1)(R_2)$, $N(R_1)(R_5)$, $N=C(R_1)(R_2)$, $N=C(R_1)(R_5)$ or has one of formula III or IV;



III



IV

each R_6, R_7, R_8, R_9 and R_{10} is, independently, hydrogen, $C(O)R_{11}$, substituted or unsubstituted C_1-C_{10} alkyl, substituted or unsubstituted C_2-C_{10} alkenyl, substituted or unsubstituted C_2-C_{10} alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the

substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally, R_7 and R_8, together form a phthalimido moiety with the nitrogen atom to which they are attached;

or optionally, R_9 and R_{10}, together form a phthalimido moiety with the nitrogen atom to which they are attached;

each R_{11} is, independently, substituted or unsubstituted C_1-C_{10} alkyl, trifluoromethyl, cyanoethyloxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

R_5 is T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a support media;

each R_1 and R_2 is, independently, H, a nitrogen protecting group, substituted or unsubstituted C_1-C_{10} alkyl, substituted or unsubstituted C_2-C_{10} alkenyl, substituted or unsubstituted C_2-C_{10} alkynyl, wherein said substitution is OR_3, SR_3, NH_3^+, $N(R_3)(R_4)$, guanidino or acyl where said acyl is an acid amide or an ester;

or R_1 and R_2, together, are a nitrogen protecting group or are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

or R_1, T and L, together, are a chemical functional group;

each R_3 and R_4 is, independently, H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_3 and R_4, together, are a nitrogen protecting group;

or R_3 and R_4 are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

Z_4 is OX, SX, or $N(X)_2$;

each X is, independently, H, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C(=NH)N(H)R_5, C(=O)N(H)R_5 or OC(=O)N(H)R_5;

R_5 is H or C_1-C_8 alkyl;

Z_1, Z_2 and Z_3 comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

Z_5 is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, N(R_1)(R_2) OR_1, halo, SR_1 or CN;

each q_1 is, independently, an integer from 1 to 10;

each q_2 is, independently, 0 or 1;

q_3 is 0 or an integer from 1 to 10;

q_4 is an integer from 1 to 10;

q_5 is from 0, 1 or 2; and

provided that when q_3 is 0, q_4 is greater than 1.

28. The method of claim 1 wherein said X_1 is Pg-O-, Pg-S-, CH_3-, CH_3-O-, morpholino or R_2R_3N- where each R_2 and R_3 is, independently, hydrogen or C_1-C_{10} alkyl.

29. The method of claim 1 wherein said Pg is CH_2CH_2CN, diphenylsilylethyl, δ-cyanobutenyl, cyano *p*-xylyl, methyl-N-trifluoroacetyl ethyl or acetoxy phenoxy ethyl.

30. The method of claim 1 wherein said heterocyclic base moiety is adenine, N^6-benzoyladenine, cytosine, N^4-benzoylcytosine, 5-methylcytosine, N^4-benzoyl-5-methyl-cytosine, thymine, uracil, guanine, N^2-isobutyrylguanine or 2-aminoadenine.

31. The method of claim 1 wherein said support media bound nucleoside, nucleotide, oligonucleoside or oligonucleotide is blocked at reactive sites.

32. The method of claim 1 wherein said blocking groups are acid stable.

33. The method of claim 1 wherein said blocking groups are base labile.

34. The method of claim 1 wherein said deprotecting reagent is acidic, neutral or basic.

35. The method of claim 32 wherein said deprotecting reagent is dichloroacetic acid, trichloroacetic acid, zinc bromide, $AlCl_3$, $TiCl_4$, (Et)AlCl, $(i\text{-Bu})_2AlCl$, ceric ammonium nitrate, 1,1,1,3,3,3-hexafluoro-2-propanol or diethyloxomalonate.

36. The method of claim 35 wherein said deprotecting reagent is 2-5% dichloroacetic acid in dichloromethane or dichloroethane.

37. The method of claim 1 wherein said deprotecting reagent is a fluoride moiety.

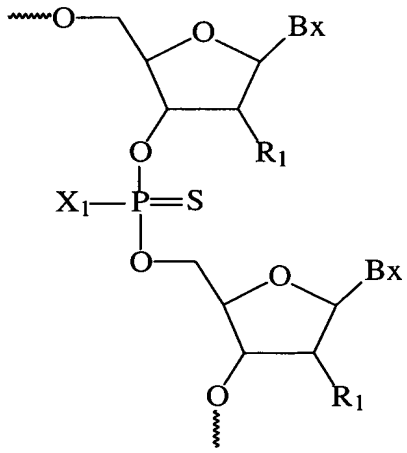
38. The method of claim 37 wherein said fluoride moiety is BF_3-etherate.

39. The method of claim 1 wherein said oligomeric compound comprises from 5 to about 50 nucleosides.

40. The method of claim 1 wherein said oligomeric compound comprises from 8 to about 30 nucleosides.

41. The method of claim 1 wherein said oligomeric compound comprises from 15 to about 25 nucleosides.

42. A method of preparing an oligomeric compound having at least one moiety of formula:



wherein:

X_1 is Pg-O-, Pg-S-, C_1-C_{10} straight or branched chain alkyl, $CH_3(CH_2)_{nn}$-O-, R_2R_3N- or a group remaining from coupling a chiral auxiliary;

nn is from 0 to 10;

Pg is CH_3, $-CH_2CH_2CN$, $-C(CH_3)(CH_3)-CCl_3$, $-CH_2-CCl_3$, $-CH_2CH=CH_2$, $CH_2CH_2SiCH_3$, 2-yl-ethyl phenylsulfonate, δ-cyanobutenyl, cyano *p*-xylyl, diphenylsilylethyl, 4-nitro-2-yl-ethylbenzene, 2-yl-ethyl-methyl sulfonate, methyl-N-trifluoroacetyl ethyl, acetoxy phenoxy ethyl, or a blocking group;

each R_2 and R_3 is, independently, hydrogen, C_1-C_{10} alkyl, cycloalkyl or aryl;

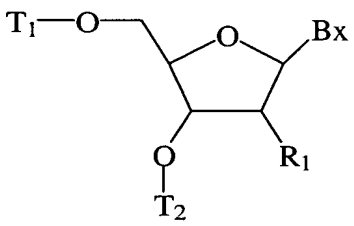
or optionally, R_2 and R_3, together with the nitrogen atom to which they are attached form a cyclic moiety that may include an additional heteroatom selected from O, S and N;

each Bx is, independently, a heterocyclic base moiety; and

each R_1 is, independently, H, a blocked hydroxyl group, or a sugar substituent group;

comprising the steps of:

(a) providing a 5'-O-protected compound of the formula:



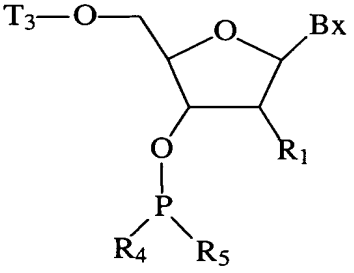
wherein:

T_1 is a hydroxyl protecting group; and

T_2 is a covalent attachment to a support media, or a support media bound nucleoside, nucleotide, oligonucleoside or oligonucleotide;

(b) treating said 5'-O-protected compound with a deprotecting reagent for a time and under conditions effective to form a 5'-O-deprotected compound;

(c) coupling said 5'-O-deprotected compound with an activated phosphorus composition of the formula:



wherein:

T_3 is a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleoside or an oligonucleotide;

R_4 is $N(L_1)L_2$;

each L_1 and L_2 is, independently, C_{1-6} straight or branched alkyl, or a C_{5-7} cyclic aliphatic ring system;

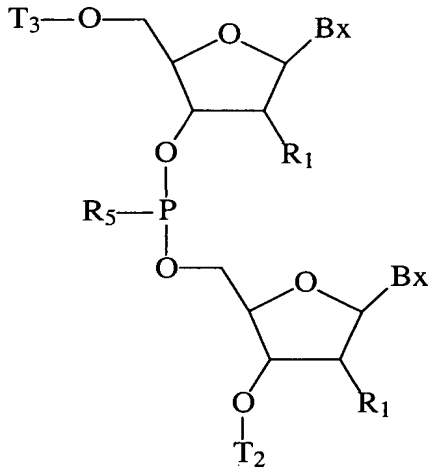
or L_1 and L_2 are joined together to form a 4- to 13-membered heterocyclic ring system including the nitrogen atom

to which L_1 and L_2 are attached, wherein said ring system optionally includes at least one additional heteroatom selected from O, N and S; and

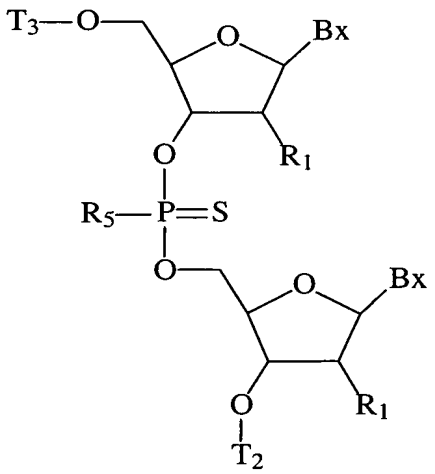
R_5 is X_1;

or R_4 and R_5 together with the phosphorus atom to which R_4 and R_5 are attached form a chiral auxiliary;

for a time and under conditions effective to form an extended compound having the formula:



(d) treating said extended compound with dimethylthiuram disulfide in a solvent thereby forming a sulfurized compound having the formula:



(e) treating said sulfurized compound with a capping reagent for a time and under conditions effective to form said oligomeric compound.

43. The method of claim 42 further comprising treating the oligomeric compound with a reagent for a time and under conditions effective to remove said blocking groups thereby forming a deblocked oligomeric compound.

44. The method of claim 43 wherein said reagent is also effective to cleave the oligomeric compound from the support media.

45. The method of claim 44 wherein said reagent is aqueous ammonium hydroxide.

46. The method of claim 43 further comprising treating said oligomeric compound with a further reagent for a time and under conditions effective to cleave the oligomeric compound from the support media.

47. The method of claim 42 further comprising treating said oligomeric compound with a deprotecting reagent for a time and under conditions effective to deprotect the T_3 hydroxyl protecting group.

48. The method of claim 42 wherein said capping reagent comprises about one part by volume of either acetic anhydride in acetonitrile or tetrahydrofuran; or chloroacetic anhydride in acetonitrile or tetrahydrofuran; added to about one part by volume of either N-methylimidazole and pyridine in acetonitrile or tetrahydrofuran; or *t*-butylphenoxyacetic anhydride in acetonitrile or tetrahydrofuran.

49. The method of claim 48 wherein said capping reagent comprises about equal volumes of 20% acetic anhydride in acetonitrile mixed with a solution having 20% N-methylimidazole, 30% pyridine and 50% acetonitrile.

50. The method of claim 42 wherein said solvent is acetonitrile, toluene, ethyl acetate, tetrahydrofuran, dichloromethane, dichloroethane, dioxane, dimethylacetamide and dimethylformamide.

51. The method of claim 42 wherein said coupling of the 5'-O-deprotected compound with the activated phosphorus composition is performed in the presence of an activating agent.

52. The method of claim 51 wherein said activating agent is 1-H-tetrazole or 4,5-dicyanoimidazole.

53. The method of claim 42 where said cyclic moiety is morpholino or phthalimido.

54. The method of claim 42 wherein each L_1 and L_2 is, independently, C_{1-6} alkyl.

55. The method of claim 54 wherein each L_1 and L_2 is isopropyl.

56. The method of claim 42 wherein L_1 and L_2 are joined together to form a heterocyclic ring system including the nitrogen atom to which said L_1 and L_2 are attached, wherein said ring system optionally includes at least one additional heteroatom selected from O, N and S.

57. The method of claim 42 wherein said X_1 is Pg-O-, Pg-S-, $-CH_3$, CH_3-O-, morpholino or $-NR_2R_3$ where each R_2 and R_3 is, independently, hydrogen or C_1-C_{10} alkyl.

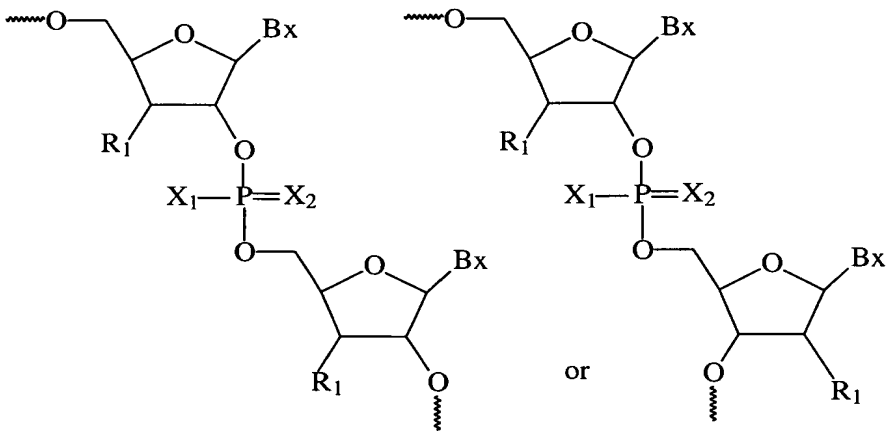
58. The method of claim 42 wherein said Pg is CH_2CH_2CN, diphenylsilylethyl, δ-cyanobutenyl, cyano *p*-xylyl, methyl-N-trifluoroacetyl ethyl or acetoxy phenoxy ethyl.

59. The method of claim 42 wherein said heterocyclic base moiety is adenine, N^6-benzoyladenine, cytosine, N^4-benzoylcytosine, 5-methylcytosine, N^4-benzoyl-5-methyl-cytosine, thymine, uracil, guanine, N^2-isobutyrylguanine or 2-aminoadenine.

60. The method of claim 42 wherein said dimethylthiuram disulfide is from about 0.02M to about 0.2M in said solvent.

61. The method of claim 60 wherein said dimethylthiuram disulfide is from about 0.1M to about 0.2M in said solvent.

62. A method of preparing an oligomeric compound having at least one moiety of one of the formulas:



wherein

X_2 is O or S;

X_1 is Pg-O-, Pg-S-, C_1-C_{10} straight or branched chain alkyl, $CH_3(CH_2)_{nn}$-O-, R_2R_3N- or a group remaining from coupling a chiral auxiliary;

nn is from 0 to 10;

Pg is CH_3, $-CH_2CH_2CN$, $-C(CH_3)(CH_3)-CCl_3$, $-CH_2-CCl_3$, $-CH_2CH=CH_2$, $CH_2CH_2SiCH_3$, 2-yl-ethyl phenylsulfonate, δ-cyano-butenyl, cyano *p*-xylyl, diphenylsilylethyl, 4-nitro-2-yl-ethylbenzene, 2-yl-ethyl-methyl sulfonate, methyl-N-tri-fluoroacetyl ethyl, acetoxy phenoxy ethyl, or a blocking group;

each R_2 and R_3 is, independently, hydrogen, C_1-C_{10} alkyl, cycloalkyl or aryl;

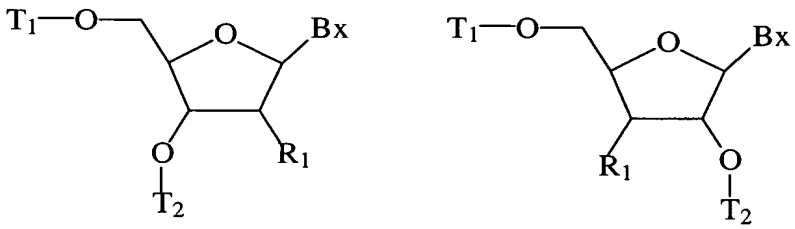
or optionally, R_2 and R_3, together with the nitrogen atom to which they are attached form a cyclic moiety that may include an additional heteroatom selected from O, S and N;

each Bx is, independently, a heterocyclic base moiety; and

each R_1 is, independently, H, a blocked hydroxyl group, or a sugar substituent group;

comprising the steps of:

(a) providing a 5'-O-protected compound having one of the formulas:



or

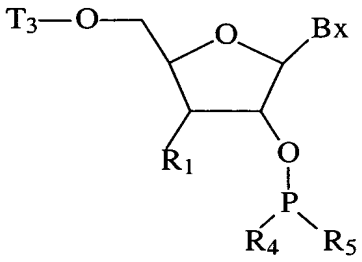
wherein:

T_1 is a hydroxyl protecting group; and

T_2 is a covalent attachment to a support media, or a support media bound nucleoside, nucleotide, oligonucleoside or oligonucleotide;

(b) treating said 5'-O-protected compound with a deprotecting reagent for a time and under conditions effective to form a 5'-O-deprotected compound;

(c) coupling said 5'-O-deprotected compound with an activated phosphorus composition of the formula:



wherein:

T_3 is a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleoside or an oligonucleotide;

R_4 is $N(L_1)L_2$;

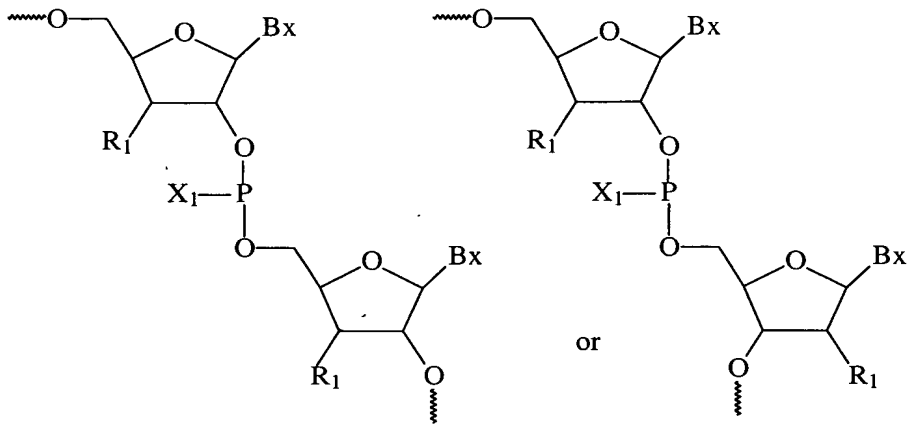
each L_1 and L_2 is, independently, C_{1-6} straight or branched alkyl, or a C_{5-7} cyclic aliphatic ring system;

or L_1 and L_2 are joined together to form a 4- to 13-membered heterocyclic ring system including the nitrogen atom to which L_1 and L_2 are attached, wherein said ring system optionally includes at least one additional heteroatom selected from O, N and S; and

R_5 is X_1;

or R_4 and R_5 together with the phosphorus atom to which R_4 and R_5 are attached form a chiral auxiliary;

for a time and under conditions effective to form an extended compound having one of the formulas:



and

(d) treating said extended compound with a mixture comprising an oxidizing reagent and a capping reagent for a time and under conditions effective to form said oligomeric compound.

63. A synthetic process comprising:

- adding methylamine, carbon disulfide and an organic solvent to a basic aqueous solution, thereby forming a mixture;
- adding ice and acid to said mixture, thereby forming an acidified mixture;
- adding an oxidizing agent to said acidified mixture, thereby forming an oxidized mixture;
- adding a non-polar solvent to said oxidized mixture, thereby forming a precipitate;
- isolating said precipitate; and
- washing said precipitate with aqueous acid and a non-polar organic solvent.

64. The process of claim 63 wherein said basic aqueous solution is maintained at about 0°C during said addition of methylamine, carbon disulfide and organic solvent.

65. The process of claim 63 wherein said acidified mixture is maintained at about 0°C to about 5°C during said addition of said oxidizing agent.

66. The process of claim 63 wherein said basic aqueous solution is aqueous sodium hydroxide.

67. The process of claim 66 wherein said sodium hydroxide has a concentration of about 2 to about 6 molar.

68. The process of claim 66 wherein the concentration of said sodium hydroxide is about 4 molar.

69. The process of claim 63 wherein said methylamine is added as an aqueous solution having a concentration of methylamine of about 1 to about 3M.

70. The process of claim 69 wherein said concentration of the methylamine is about 2M.

71. The process of claim 63 wherein said organic solvent is tetrahydrofuran.

72. The process of claim 63 wherein said acid is glacial acetic acid.

73. The process of claim 63 wherein said acid is added to give a final pH of about 1 to about 6.

74. The process of claim 63 wherein said oxidizing agent comprises aqueous hydrogen peroxide.

75. The process of claim 74 wherein said hydrogen peroxide has a concentration of about 10 to about 30%.

76. The process of claim 75 wherein the concentration of said hydrogen peroxide is about 30%.

77. The process of claim 63 wherein said non-polar organic solvent is hexanes or heptane.

78. The process of claim 63 wherein said aqueous acid is trichloroacetic acid.